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**Modeling Effects of Immunosuppressive Drugs on Human Hearts Using Induced Pluripotent Stem Cell-Derived Cardiac Organoids and Single-Cell RNA Sequencing.**

**Journal:** Circulation

**Publication Year:** 2022

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**PubMed link:** 35467958

**Funding Grants:** CIRM Bridges 2.0: Training the Next Generation of Stem Cell Scientists

**Public Summary:**

We examined the cardiovascular effects of tacrolimus and sirolimus by using a human induced pluripotent stem cell-derived cardiac organoid model after comparing clinical phenotypes associated with each drug. Methods are available on request from the corresponding authors. Institutional review board approval was obtained for all experiments and human subjects signed informed consent. We first evaluated cardiac graft remodeling by examining changes in left ventricular (LV) mass between 6 and 30 months after transplant using serial echocardiographic evaluations (Figure A). We grouped patients by primary immunosuppression agent. We observed a statistically significant reduction in LV mass over time in the sirolimus group (reduction of 19.91 g, 95% CI reduction of 25.6 g to 7.85 g) compared with the tacrolimus group (reduction of 3.62 g, 95% CI reduction of 12.48 g to increase of 7.41 g). Increase in LV mass is a feature of adverse remodeling that may contribute to diastolic dysfunction and cardiac graft dysfunction. Our findings are consistent with other reports that observed a favorable cardiac remodeling profile with proliferation signal inhibitors compared with calcineurin inhibitors.<sup>3</sup>

**Scientific Abstract:**

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